



...making excellence a habit.™

EU Medical Device Regulation
(current & proposed)

Comparison to US Medical
Device Regulation

EU Unannounced Visits

AFDO June 2014, Denver

Paul Brooks
Healthcare Solutions



BSI Healthcare Mission



To ensure patient safety while supporting timely access to medical device technology globally.

To provide our customers thorough, responsive, predictable conformity assessments, evaluations and certifications that are recognized and accepted worldwide.

Europe & CE Marking

- Medical device directives (AIMDD, MDD, IVDD)
 - Single common framework
 - Individual sovereign nations (Member States)
 - Transposed into national regulations
- Manufacturers regulatory staff must understand and interpret the directives
- Reimbursement varies by Member State
- Additional registration requirements in some Member States

Europe & CE Marking

- European Commission (EC)
 - Proposes and issues EU Regulations, Directives and Recommendations
 - Coordinates EU Member State Competent Authority cooperation
 - Designates Notified Bodies
 - Issues guidance documents (MEDDEV's)
 - Ensures the effective operation of the single market

Europe & CE Marking

- Competent Authority (CA)
 - Acts for each EU Member State – Regulator
 - Responsible for enforcement of regulations
 - Provides designation of Notified Bodies to the EC
 - Provide guidance and interpretation
 - Approves clinical investigations
 - Receives vigilance incidence reports and investigates
 - Responsible for safeguarding public safety
 - Conducts market surveillance

Europe & CE Marking

- Notified Body (NB)
 - Third party expert, competent certification / conformity assessment body
 - Designated by EU Member State Competent Authority
 - Conducts conformity assessment to verify manufacturers claims of compliance
 - Medical device technical documentation reviews
 - Quality systems assessments (ISO 13485)
 - Many devices can be covered under the QMS
 - Ongoing surveillance of manufacturers (annual)
 - Design dossiers examination for higher risk devices
 - Five year renewal (revisit CE Marking decisions)

EU Definitions

- Manufacturer
- Medical Device
 - AIMD, Medical Device, In Vitro Diagnostic
 - Medical purpose
- Accessory
- Placing on the Market
- Need for CE Marking
 - Custom made devices
 - Device for Clinical Investigation
- Combination Devices
 - Devices that incorporate medical substances and/or animal derived materials and/or human blood products

Europe & CE Marking

- EU Directives require
 - Classification - risk/rules based
 - Compliance with Essential Requirements
 - Harmonized standards presumption
 - Clinical evaluation
 - Technical Documentation
 - Conformity assessment based on risk (quality and/or product evaluation)
 - Post marketing activities (reactive and pro-active)
 - Declaration of conformity

Quality Assurance System Requirements

- The QS application must include the name and address of the manufacturer and any additional manufacturing site covered by the quality system.
- Application of the quality system must ensure that the products conform to the provisions of this Directive which apply to them at every stage, from design to final inspection.
- Technical documentation must include adequate description of organization of business and in particular, where the design, manufacture and/or final inspection and testing of the products, or elements thereof, is carried out by a third party, the methods of monitoring the efficient operation of the quality system and in particular the type and extent of control applied to the third party.

Quality Assurance System Requirements

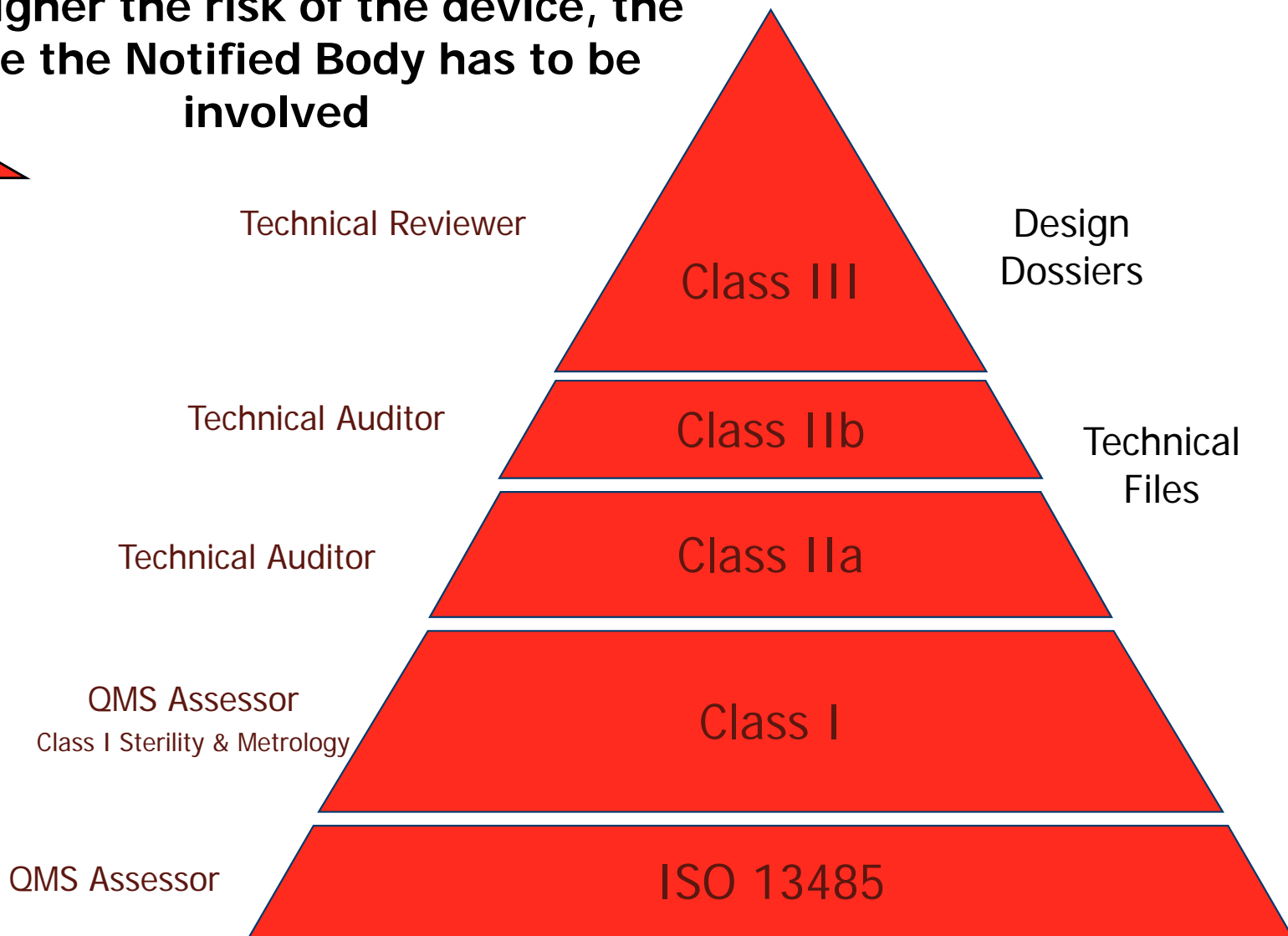
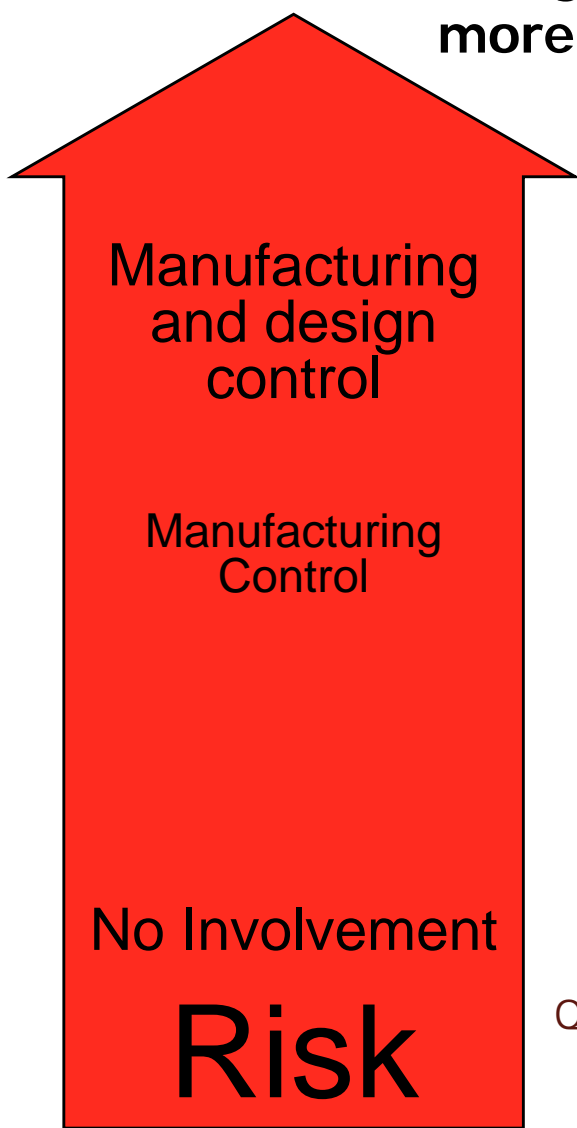
- The notified body must audit the quality system to determine whether it meets the requirements referred to in Section 3.2. It must presume that quality systems which implement the relevant harmonized standards conform to these requirements.
- EN ISO 13485:2012 provides a presumption of conformity
- The assessment team must include at least one member with past experience of assessments of the technology concerned.
- The assessment procedure must include an inspection on the manufacturer's premises and, in duly substantiated cases, on the premises of the manufacturer's suppliers and/or subcontractors to inspect the manufacturing processes.
- The decision is notified to the manufacturer. It must contain the conclusions of the inspection and a reasoned assessment.

Classification

- Risk based system
- Medical Devices Directive
 - Class I to III Rules based
- Active Implantable Medical Devices Directive
 - One class (equivalent to MDD class III)
- In Vitro Diagnostics Directive
 - List based
 - Self use

Notified Body Involvement (Under MDD)

The higher the risk of the device, the more the Notified Body has to be involved



Technical Documentation

- The requirements for the technical documentation are laid down in conformity assessment annexes of the directives
- As a general rule, the documentation should cover the design, manufacture and intended use of the product and evidence for safety and performance
- Demonstrates compliance with Essential Requirements
- Available to EU Member States
- For lay-out: GHTF doc. STED - www.gh tf.org

Technical Documentation - Content

The technical documentation must allow assessment of the conformity of the product with the requirements of the Directive. **It must include in particular:**

- general description of the product and intended use(s),
- design drawings, methods of manufacture, diagrams of components,
- explanations necessary to understand the operations of the product,
- results of the risk analysis,
- list of harmonised standards, applied in full or in part,
- descriptions of the solutions adopted to meet the ERs,
- in the case sterile products validation report,

Technical Documentation - Content

- results of the design calculations and inspections carried out,
- if the device is to be connected to other device(s), proof must be provided that it conforms to the ERs,
- solutions adopted as referred to in Annex I,
- pre-clinical evaluation,
- clinical evaluation in accordance with Annex X,
- label and instructions for use.

Technical Documentation Review

- Class I (Plus Most IVD)
 - Manufacture self-declare no Notified Body involvement
- Class IIa & Class IIb (Medium Risk IVD)
 - Manufacturer applies for a certification scope
 - Devices are divided 'device subcategory' and 'generic device group'
 - Notified body is required to sample technical documentation
 - Up to 5 year certification recommendation for the scope of devices
 - Plan to sample all 'device subcategory' and 'generic device group' over 5 year certification plan
 - Technical documentation sampled pre and post market

Class III (AIMD & High Risk IVD) Design Dossier Examination

- Full technical documentation submitted to notified body as a design dossier
 - Same technical documentation elements as class IIa/IIb
- Design dossier examined by the notified body
- Dossier should include Post Market Surveillance Plans (PMS) –including if appropriate Post Market Clinical Follow-up (PMCF)
- Five year EC Design Examination Certificate

Essential Requirements (ER)

1. Safe - benefits outweigh risk
2. State of the art - inform of residual risks
3. Perform as intended
4. Lifetime defined
5. Packaging suitable for transport and storage
6. Side effects acceptable
 - a) Clinical data evaluation

- 7 – 12. Specific
13. Labelling
- Additional:
 - applicability of the Machinery Directive (Article 3) & PPE (Article 1, clause 6)

Clinical Evaluation

- The manufacturer must have clinical data for the device for its intended use.
 - From existing equivalent data or a specific clinical investigation.
 - Clinical investigations must be conducted according to the Directive (Standards, Guidance)
- A clinical evaluation of the clinical data is required to support CE Marking.
- Post market clinical follow-up required unless otherwise justified.

MEDDEV 2.7.1 – “Equivalent Devices”

Section 5.1 – Scope of CER:

- Devices should have the **same intended use** and will need to be compared with respect to their **technical** and **biological characteristics**.
 - **Intended use** relates to the clinical condition being treated, the severity and stage of disease, the site of application to/in the body and the patient population
 - **Technical characteristics** relate to the design, specifications, physiochemical properties including energy intensity, deployment methods, critical performance requirements, principles of operation and conditions of use
 - **Biological characteristics** relate to biocompatibility of materials in contact with the same body fluids/tissues.
- Characteristics should be **similar to extent** that there would be **no clinically significant difference** in the performance and safety of the device.

MEDDEV 2.7.1 – “Equivalent Devices”

Appx. F, Sec. 3.2.3 (Footnote) – Meaning of Equivalence

- **Clinical:**

- C1 - same clinical condition or purpose
- C2 - same site in the body
- C3 - similar population (including age, anatomy, physiology)
- C4 - similar relevant critical performance for specific intended use

- **Technical:**

- T1 - similar conditions of use
- T2 - similar specifications and properties
- T3 - similar design
- T4 - similar principles of operation

- **Biological:**

- S1 - same materials in contact with the same tissues or body fluids

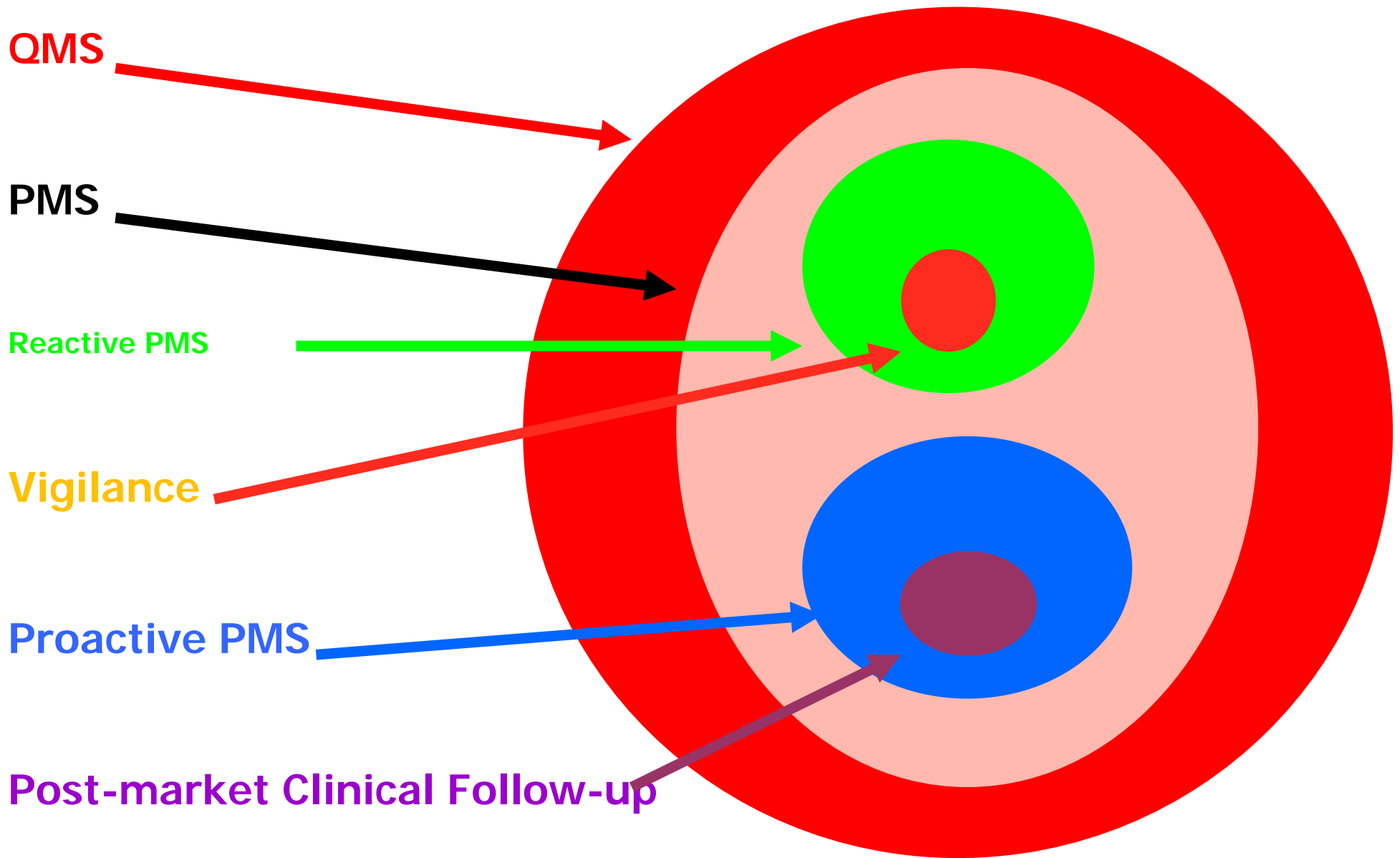
Post Market Surveillance

Manufacturers:

- must have documented an appropriate system for gaining and reviewing experience in the post-production phase from the range of devices manufactured
- should evaluate actual device experience on a more proactive basis, rather than relying on purely reactive activity
(i.e. don't just rely on customer complaints and devices problem issues)

ISO 13485: 8.2.1

ISO 14971: 9



United States Regulatory System

European Union Regulatory System

QSR - 21 CFR Part 820 Inspection by FDA	ISO 13485 QS Assessment by Notified Body (depending on classification)
PMA or 510(k) Reviewed by FDA	Technical Documentation Sampled by Notified Body (depending on classification) – Class III Design Dossier (PMS) Essential Requirements Risk Assessment Clinical Evaluation Post Market Surveillance Plans
	Manufacturers Declaration of Conformity
FDA US Market Clearance	CE Marking
MDR	Manufacturers Post Market Surveillance (including complaints and vigilance)
FDA Inspections (24 months)	Notified Body QMS Audits (Annually) Sampling of Technical Documentation
	Notified Body Recertification Every Five Years

Europe & CE Marking: Sources of Information

- European Commission
- http://ec.europa.eu/health/medical-devices/index_en.htm
- European Guidance
- http://ec.europa.eu/health/medical-devices/documents/guidelines/index_en.htm
- European Notified Body Association - *Team NB*
- <http://www.team-nb.org>
- European Association of Authorized Representatives - *EAAR*
- <http://www.earmed.org/>
- BSI
- <http://medicaldevices.bsigroup.com/en-US/>

Proposed Medical Device Regulation (MDR) & IVD Regulation (IVDR)

Caution

- The new EU regulations are not finalized and subject to change



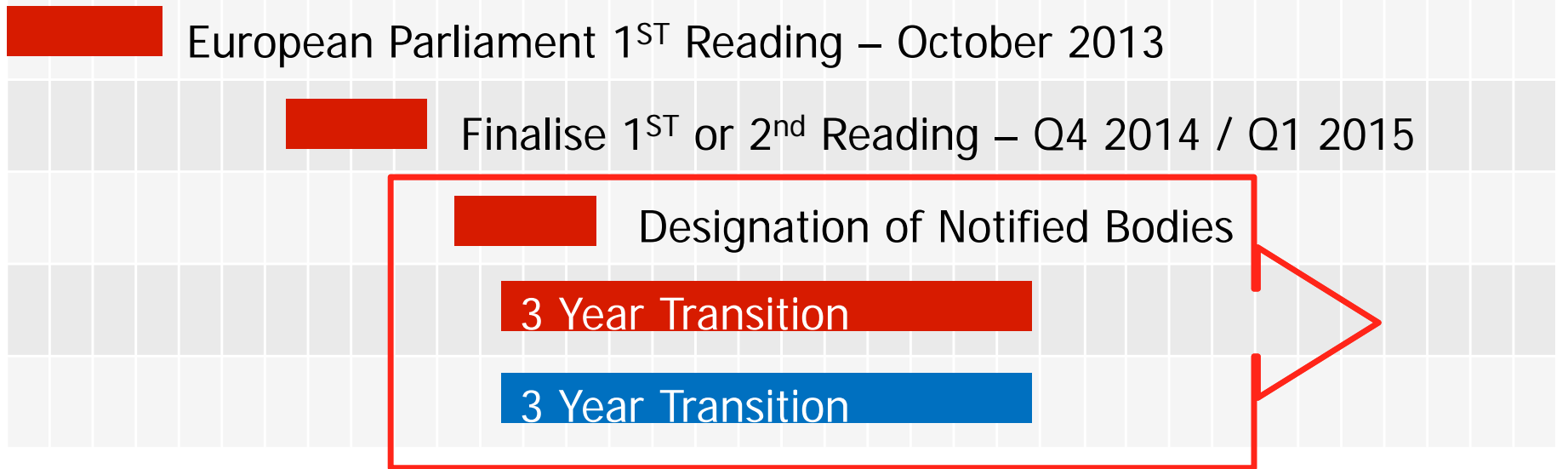
<http://www.bsigroup.com/en-GB/our-services/medical-device-services/BSI-Medical-Devices-Whitepapers/>

Three Directives become Two Regulations

- Impact of becoming a Regulation
- Direct entry into force
 - Three year transition period for MDD/AIMD
 - Three year transition period for IVD
- Regulation should result in more consistent application
- Appropriate legal instrument that imposes clear & detailed rules which become applicable in a uniform manner and at the same time throughout the EU

Timelines

2013				2014				2015				2016				2017				2018				2019				2020				2021							
Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q
1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4



■ Regulation covering MD & AIMD
 ■ Regulation covering IVD

Delegated Entities under the Proposed Regulation

- European Commission (EC)
- EU Member States (MS)
- EU Competent Authorities (CA)
- Medical Device Coordination Group (MDCG)
- Medical Device Advisory Committee (MDAC)
- Assessment Committee for Medical Devices (ACMD)
- EU Reference Laboratories (EURL)
- European Medicines Agency (EMA)
- Notified Bodies (NB)
- Special Notified Bodies (SNB)

Single-Use Devices – Big Debate

- *Hot political discussion – Final position TBD*
- *Single-use device – ‘...has been tested and demonstrated impossible to reuse.’*
- *Devices labeled as single-use should really be single-use*
- *All devices should be reusable as a rule, unless they are on a list established by the EC after consultation with MDAC*
- *Reusable device – ‘...suitable for reprocessing’ for multiple patients/procedures*

Economic Operators

Manufacturer

means the natural or legal person who manufactures or fully refurbishes a device or has a device designed, manufactured or fully refurbished, and markets that device under his name or trademark

Importer

means any natural or legal person established within the Union who places a device from a third country on the Union market

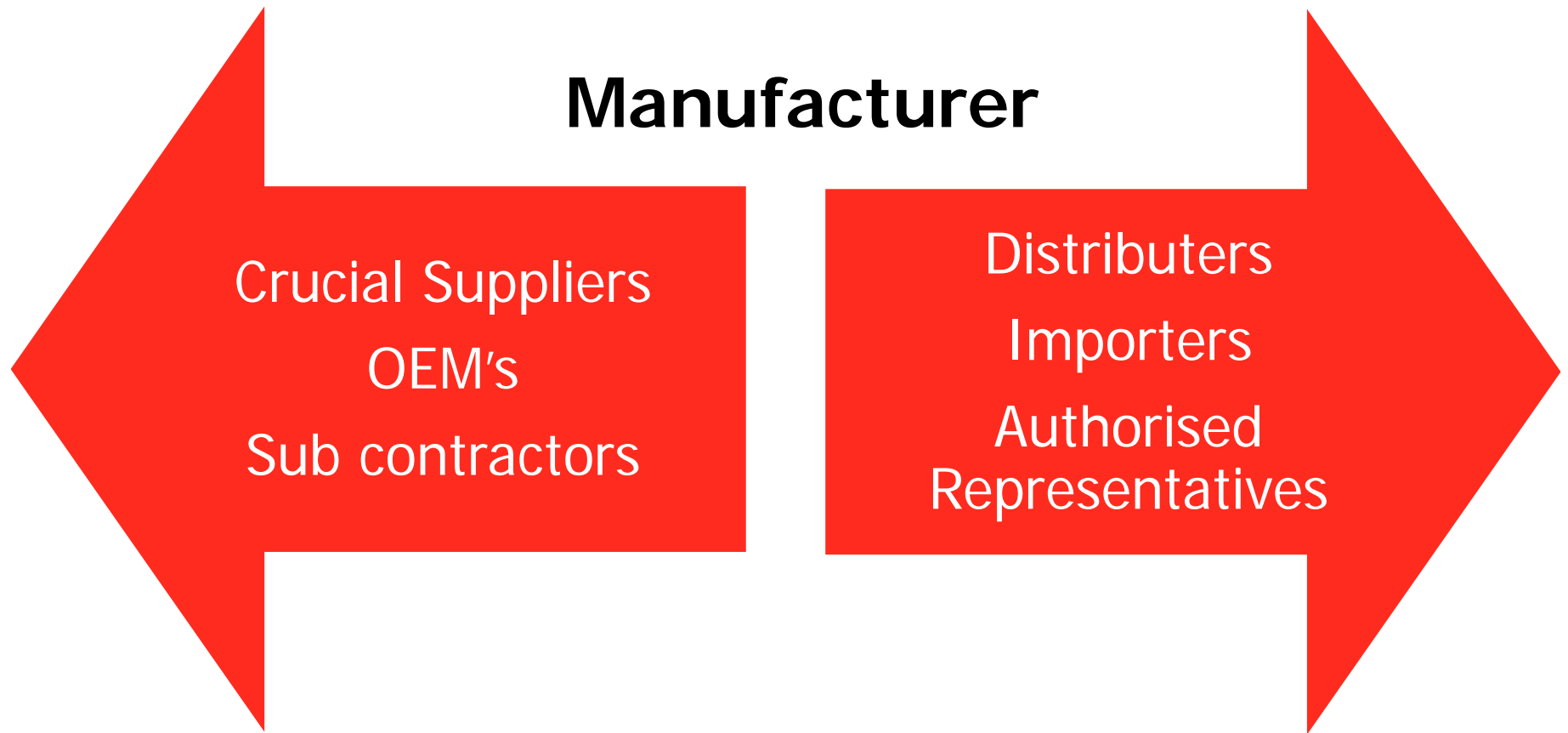
Distributor

means any natural or legal person in the supply chain, other than the manufacturer or the importer, who makes a device available on the market

Economic operators

means the manufacturer, the authorised representative, the importer and the distributor

Increased Control of the Supply Chain



Eudamed: European Electronic Database

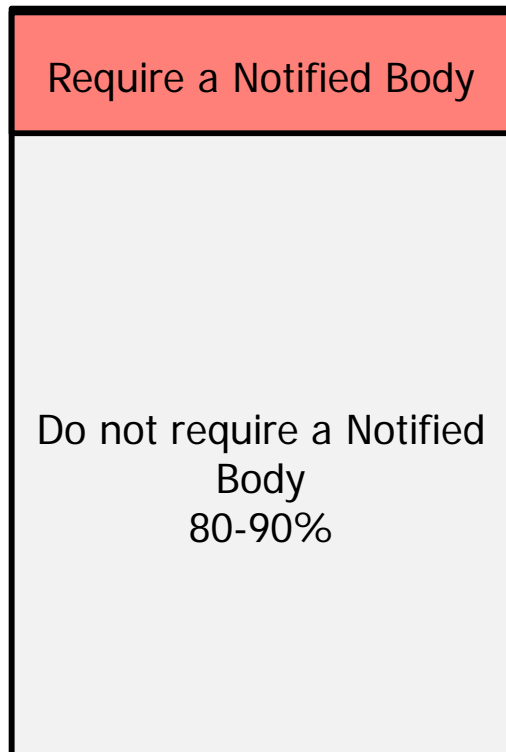
- UDI
- Registration of devices and economic operators
- Information of certificates
- Clinical investigations
- Vigilance
- Market surveillance
- Public access
 - Allow comparison of devices, economic operators, clinical investigations, vigilance

Person Responsible for Regulatory Compliance

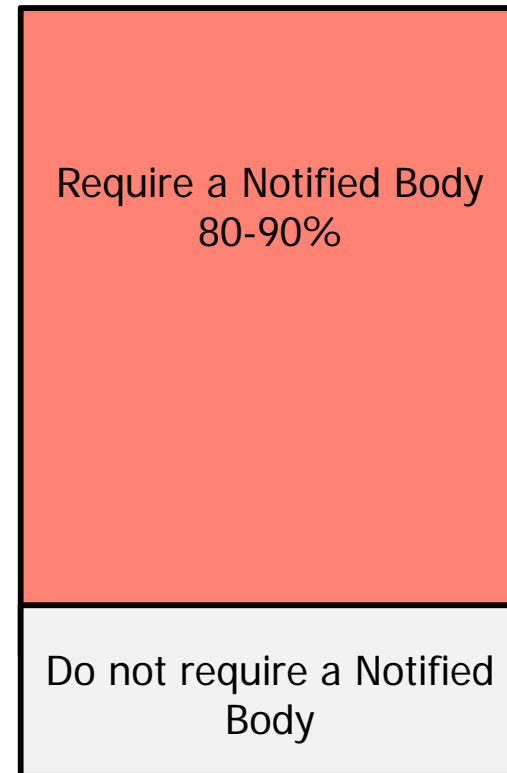
- Manufacturers within their organisation at least one qualified person who possesses expert knowledge in the field of in vitro diagnostic or medical devices. This will include:
 - a degree or equivalent in natural sciences, medicine, pharmacy, engineering, law plus at least two years of professional experience in regulatory affairs or in QMS in medical devices or IVD's or
 - Three years of professional experience in regulatory affairs or in QMS relating to medical devices or IVD's
- Responsible for ensuring:
 - that the conformity of the devices is appropriately assessed before a batch is released
 - that the technical documentation and the declaration of conformity are drawn up and kept up-to-date
 - that vigilance requirements have been fulfilled
 - Subjects in clinical investigations or performance evaluation for interventional studies
- The qualified person should suffer no disadvantage by performing their duties
- Authorised representatives will also be required to have person responsible for regulatory compliance

Quantum Leap for IVD's

IVD Directive



IVD Regulation



Safety and Clinical Performance Report

- For all class III and implantable device
- Based on data collected during the clinical investigation
- Submitted to Special Notified Body for review
- Special Notified Body will validate
- Must be understandable by users in the relevant local MS language
- The summary will be made available to the public through Eudamed
- Safety and clinical performance report shall be updated annually with clinical evaluation reports

Implant Card and Information about Implantable Devices

- Manufacturers of implantable devices shall provide implant card for particular patients
 - Implant card shall also be made available in an electronic format
 - Identifies device implanted including UDI
 - Warning, precautions, measures to be taken with reciprocal interference with external influences (e.g. compatibility with diagnostic devices)
 - Potential adverse effects
 - Information on expected life cycle and follow-up
 - Principal characteristics of device including materials
- Exempted implants: sutures, staples, dental implants, screws, plates

New EU Unannounced Visits



RECOMMENDATIONS

COMMISSION RECOMMENDATION

of 24 September 2013

on the audits and assessments performed by notified bodies in the field of medical devices

(Text with EEA relevance)

(2013/473/EU)

THE EUROPEAN COMMISSION,

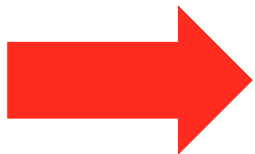
legal obligations, notified bodies should perform unannounced audits in addition to product assessments and quality system assessments.

Where will we visit ?

Legal

Manufacturer?

YES if all or some manufacturing , design or test activities performed onsite for all or some products



Significant Subcontractor or Crucial Supplier?

YES, for virtual manufacturers

Where will we visit?

“...if this is likely to ensure more efficient control... in particular if the main part of the design development, manufacturing, testing or another crucial process is located with the subcontractor or supplier.”

Critical Subcontractor

E.g. Manufacturer of significant components, regulatory responsibility and / or activities essential for ensuring compliance with legal requirements. Design or software development, sterilisation, sterile packaging.

Crucial Supplier

E.g. Manufacturer of finished devices, key sub-assembly. Critical raw materials such as silicone gel component for an implant, animal tissue for use in heart valve.

How often?

Per the Commission Recommendation & NB Code of Conduct

Minimum frequency in number of years for an unannounced visit	Classification			
	I	IIa	IIb <i>Annex II List B</i>	III / AIMD <i>Annex II List A</i>
Normal conditions	3 yrs	3 yrs	3 yrs	2 yrs
Devices that are often non-compliant	2 yr	2 yr	1 yr	1 yr
Specific reasons for suspicion	2 yr	2 yr	1 yr	1 yr

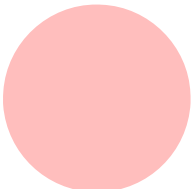
As frequently as needed

For how long?

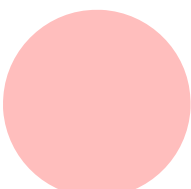
- Most Manufacturers
 - Including small & medium sized facilities
 - One day by two auditors
- Very Large Manufacturers
 - Several hundred employees +
 - Four man-days (or more in extreme cases). Likely two assessors for two days
 - Or an increase in frequency of visits



What will happen on the day?



BSI Assessors arrive onsite and present identification
Request to speak to allocated contact or the most senior person on site
Brief explanation of visit, but no formal opening meeting



Audit team progress swiftly to manufacturing area
Assessment team work together to audit all elements specified in the Commission Recommendation and identify areas / processes for further audit as part of the visit



Brief closing meeting, with details of findings where possible
Report will be provided within approximately one week
Follow up of any non-conformities through normal audit processes

Any Questions



Paul Brooks

Senior Vice President Healthcare Solutions

+1-703-464-1923

Paul.Brooks@BSIGroup.com

<http://medicaldevices.bsigroup.com/>

<http://medicaldevices.bsigroup.com/en-US/Our-services/Unannounced-audits-from-BSI/>

bsi.

...making excellence a habit.™